

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
9 November 2000 (09.11.2000)

PCT

(10) International Publication Number  
**WO 00/66713 A3**

(51) International Patent Classification<sup>7</sup>: C12N 5/06, 5/08,  
5/10, A61K 35/30, G01N 33/50, C12Q 1/68

(21) International Application Number: PCT/EP00/03842

(22) International Filing Date: 27 April 2000 (27.04.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/132,317 3 May 1999 (03.05.1999) US

(71) Applicant (*for all designated States except US*):  
**KAROLINSKA INNOVATIONS AB** [SE/SE]; Tomte-  
bodavägen 11, F, Solna, S-171 77 Stockholm (SE).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **ARENAS, Ernest**  
[ES/SE]; Laboratory of Molecular Neurobiology, Depart-  
ment of Medical Biochemistry and Biophysics, Karolinska  
Institute, S-171 77 Stockholm (SE). **PERLMANN,**  
**Thomas** [SE/SE]; The Ludwig Institute for Cancer  
Research, Stockholm Branch, Karolinska Institute, P.O.  
Box 240, S-171 77 Stockholm (SE). **SNYDER, Evan,**  
**Y.** [US/US]; Departments of Neurology and Pediatrics,  
Harvard Medical School and Division of, Neuroscience,  
Children's Hospital, 320 Longwood Avenue, Boston, MA  
02115 (US). **WAGNER, Joseph** [US/SE]; Laboratory of  
Molecular Neurobiology, Department of Medical Bio-  
chemistry and Biophysics, Karolinska Institute, S-171 77

Stockholm (SE). **ÅKERUD, Peter** [SE/SE]; Laboratory  
of Molecular Neurobiology, Department of Medical Bio-  
chemistry and Biophysics, Karolinska Institute, S-171 77  
Stockholm (SE).

(74) Agents: **WALTON, Seán, M.** et al.; Mewburn Ellis, York  
House, 23 Kingsway, London WC2B 6HP (GB).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,  
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,  
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,  
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent  
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent  
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,  
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,  
GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

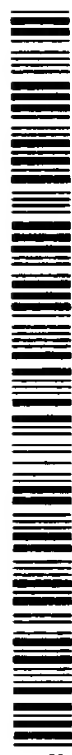
*With international search report.*

(88) Date of publication of the international search report:  
5 April 2001

*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: MATERIALS AND METHODS RELATING TO NEURONAL DEVELOPMENT

(57) Abstract: The invention relates to the induction of the neuronal fate in neural stem cells or neural progenitor cells. The inventors have found that a neuronal fate in a neural stem cell or neural progenitor cell can be induced by expressing *Nurr1* above basal levels within the cell. *Nurr1* is a transcription factor of the thyroid hormone/retinoic acid nuclear receptor superfamily. It is shown herein that the expression of *Nurr1* above basal levels in neural stem cells or neural progenitor cells increases the proportion of the cells which differentiate toward a neural fate. It has been found that in particular, dopaminergic neural stem cells or progenitor cells by a process including expression of *Nurr1* above basal levels in the cells and contact of the cells with one or more factors supplied by or derived from Type I astrocytes of the ventral mesencephalon.



WO 00/66713 A3